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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/696,801 | 10/25/2000 | Lee A. Bulla JR. | 48279-3USPT | 3203 |

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Morrison & Foerster
3811 Valley Centre Drive
Suite 500
San Diego, CA 92130

| EXAMINER | |
|---|---|
| CLOW, LORI A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1631 | 18 |

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Offic Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/696,801 | BULLA ET AL. | |
| | Examiner | Art Unit | |
| | Lori A. Clow, Ph.D. | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-19,23,25,26,34,36-41,45,47,48,60-62,64-66,70,72,73,81 and 82* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-19,23,25,26,34,36-41,45,47,48,60-62,64-66,70,72,73,81 and 82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Applicants' arguments, filed 30 September 2002, have been fully considered by they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. Claims 13-19, 23, 25, 26, 34, 36-41, 45, 47, 48, 60-62, 64-66, 70, 72, 73, 81, and 82 are currently pending. Applicant is requested to cancel claims 1-12, as they are directed to non-elected subject matter.

### *Drawings*

Applicant did not fix the drawings as required by form PTO 948 in the Office Action mailed 2 November 2002. Applicant is hereby notified that the required timing for the correction of drawings has changed. Due to the above notification Applicant is required to submit drawing corrections within the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

### *Claim Rejections - 35 USC § 112*

Claims 13-19, 23, 25, 26, 34, 36-41, 45, 47, 48, 60-62, 64-66, 70, 72, 73, 81, and 82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 13, 60, and dependent claims recite "comparing the second nucleotide sequence to nucleotide sequences catalogued in one or more databases that correlate nucleotide sequences with phenotypic characteristics." The specification, however, does not indicate that there are databases utilized that are capable of correlating sequences with phenotypic data. In fact, databases merely hold information and correlation would be performed utilizing a search program.

Claim 14 and dependent claims introduce "filtering the extracted nucleotide sequences to eliminate portions common to unwanted genes." However, the specification does not describe, nor was it originally claimed that filtering the extracted nucleotide sequence would "eliminate portions common to unwanted genes." The specification, on page 20, only refers to filtering repetitive sequences and there is no basis for filtering out unwanted or undesired genes.

Claim 34 and dependent claims introduce " a system...comprising one or more computers ...a communication link...etc." However, the claims as originally filed read on and the specification describes sequences that are compared utilizing the information in various databases that provide sequences of species genomes. Nowhere is it mentioned that this comparison is done via a network with communication links between computers nor is it stated that one or more computers would be linked.

For each of these limitations, applicant is requested to point to specific page and line numbers for support.

Claims 13-19, 23, 25, 26, 34, 36-41, 45, 47, 48, 60-62, 64-66, 70, 72, 73, 81, and 82 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to design primers to amplify a target sequence with at least one known phenotypic characteristic based upon another known sequence with that characteristic, as recited in claim 13. The steps include providing sequences, comparing sequences from databases, extracting gene sequences that have desired phenotypic characteristics, aligning these with known sequences, prioritizing those sequences, and design primers to target sequences based upon above steps. For the reasons discussed below, however, the specification provides insufficient guidance in order to practice the invention.

b) and c) In the first step of base claim 13, a method to design primers to target a first nucleotide sequence that results in at least one phenotypic characteristic is described. However, the specification does not provide for a definition, other than expression in midgut, of phenotypic

characteristics. On pages 47 and 59 and in figure 2, there are no explanations as to how a target is selected from one or more databases based upon expression phenotype. In general, phenotypes are much broader than just defined as expressed or not expressed and cannot generally be defined by one gene. Albeit, the specification still does not provide guidance in terms of picking out genes according to the phenotype of expression in mid-gut and thus undue experimentation would be required in order to practice said invention.

In the second step of claim 13, a comparison between known sequences and sequences catalogued in databases is required, followed by extracting gene sequences with a characteristic in the known sequence, prioritizing these sequences, and aligning these. The specification provides general examples for using publicly available search and alignment programs (BLAST, pages 14-20; Clustal W, pages 20-25; Acedb, pages 25-27) to align known sequences of interest (i.e. with phenotypically desirable characteristics) and extract prioritized sequences in order to compare these sequences with target sequences so that primers may be designed. In addition to the publicly available databases listed above, Tables I-IX recite numerous sequence retrieval-interface, comparison, searching, assembly, primer design, etc. software tools that may be utilized in this invention (pages 27-57). The specification provides a working example using one of these available programs to target a membrane protein involved in cytoskeletal formation (beta integrins), originally identified in *Manduca sexta.* These were run against all organisms from the PubMed database. Beta integrin proteins that were identified from all organisms were then aligned; primer selection was made utilizing MacVector software; and *M. sexta* products were cloned (see example 1, page 59). It is noted that the primer design was performed by

software well known in the art at the time of invention. However, the primer design described was not practiced following the claimed method.

In addition, the specification does not provide for sequences that contain "a portion of the nucleotide sequences". How large or small must this portion be? What criteria are used to determine this? Furthermore, how is it known that the sequence which is extracted will have the phenotypic characteristic.

Furthermore, gene sequences are prioritized based upon what condition? There are no steps in the examples to illustrate prioritization of sequences. Nor are there steps that are active that would direct one to design primers based upon the matching portions of the alleged prioritized sequences. The inclusion of the software MacVector in the examples is not directive. Software versions change, as do the parameters that run them.

Absent clear and illustrative guidance as to how to particularly perform the above invention, there would be undue experimentation required in order to practice the specific steps of the invention.

d) The invention is drawn to methods to design primers that amplify a desired phenotype in an unknown target sequence based upon that which is known for a second sequence.

e) and g) It would have been well known in the art that there are numerous programs publicly and privately available to perform the steps of sequence searching (i.e. BLAST), alignment (i.e. Clustal W), primer design (i.e. MacVector), etc. as recited in the above said invention. However, the mere use of these available programs does not provide guidance that enables one of skill in the art to practice said invention without undue experimentation. There is

no guidance on how to integrate the various software products in order to practice the claimed invention.

f) The skill of those in the art of molecular biology is high.

The skilled practitioner would first turn to the instant specification for guidance to practice methods of primer design. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that there are numerous programs that could perform various parts of the method. The specification is an invitation to experiment, as it requires one of ordinary skill in the art to determine how to integrate various pieces of known software, including determining cut-offs, thresholds, parameters, in order to practice the claimed invention. This is undue experimentation. A general method concept is disclosed without ever providing sufficient instruction or guidance to permit implementation.

Claims 13, 16, 18, and dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 and dependent claims recite "a method to design primers...that result in at least..." This language is confusing in that how could a method to design primers result in a phenotype? Perhaps applicant meant a method to design primers having at least one phenotypic characteristic?

Claim 16 recites a step of cloning genetic material using one or more designed primers. However, claim 13, from which it depends, recites the intended use of this claim as designing primers and NOT cloning. The step of cloning changes the intention of the claim.

No claim is allowed.

***Inquiries***

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800
AU1631

December 10, 2002

Lori A. Clow, Ph.D.
Art Unit 1631
Lori A. Clow